

Figure 1

A. HDAC4

MSQSHPGCLSGRDQFVELLNPARYARHPSTVDVATLPQVAPSAVPHDLRHDQFSLPVAEPALRECOLOELLALXKQKQI0R0ILI 90  
AEFORQHEQLSRQCAQLHEHIXQOQDLAMHQOELLEHQRKLERHROEQELEKHREQQLQLOKKEKESAVASTEVOXKLQEFVL 180  
NKXGALAHNRHNCISSDPRTYTKGTQKSSLDQSSPPQSGVSTSYNHPVLQYDADDFLRXTASEPHLQSRSLQKVAERSSPLL 270  
KDCGPVYVATLXKRPDLVDTGACSSAPGSSPNNSSGVSSENGIAPAVPSTPAETSLAHLVAREGSAAPLPLTSPSLPWTITCLPA 360  
TQPSMAGQOQDTERLTPALQORSLFPGTHLTPYLTSTPLERDGGANISFLQHPMLLEQPPAQAPLVTCLALPLDQSLVADRVS 450  
PSIHLPKRRPLGCTOSAPLPQMAQALQNVITQOQOQOFLERQO 540  
LDRLPQCEAHQAQGVQVQKQPIESDEEEAEFPRVEFGQRQPSQELLFROQALLLEDQRIHQUNYQASHEAAGIPVSPGGRPLSRA 630  
QSSPASATFPVSQEPPTXPRFTTGLVYDTLHLHQCTCGSSSSHPDHAGRIQSIHSLQETCLAGQCECIRGRXATLEELQTVHSEAH 720  
LLYGTNPLNRKLDKSLGSLASVFLPCGCVGVDSDTTIWEHVSAGAAVLAVCCVVELVFKVATGELONGFAVVRPGBRAESTPM 810  
GPTTNCVAVPAALQORLSYSKILTVMDVIBGNGTQAVTESDPSVLYSHLRYDQOFFPGSCAFDEVTGTCVGFNVHAPTCGLP 900  
PKDASYLANFTVMPPLASFPAPVLYSSCFDAVCHFTPLQCTNLSARCTGYLTQKHLGACGRIVLALDGGDLTALCDASEACVS 990  
ALLQHELDPLPEKVLQORPHANAVRSEKVMHISYHRCLOTTITAGRSLEIAGTCNEEAETVTHASLSVGVKPAEDRPDEEPHEE 1080  
EPPL. 1085

B. HDAC5

MSNPESDCHSGREPSLEITLPTSLHSIPVTVEVQVLPFRMPSSKCGGGGSPSPVELGALVGVDPITLREQOLOELLALXKQOQLQ 90  
KQLLFAEFQKHDELTRQHEVOLQKRLQOQDLAAQOQDLAAQOQDLAAQOQDLAAQOQDLAAQOQDLAAQOQDLAAQOQDLAAQOQDL 180  
TEVKLRQEFLLSKKEPTPOGLNLSLPHKPCGABASLDQSSPPQSGPPGTPPSYKLPLGPFYDSDDFLRKTASEPMLVSRILX 270  
QKVAERSSPLLKDDGTVISTFQDAVEITCAGPAASSVCHSAPGSSPNNSSSTIADGFTCSVPVPIITMLPCHRALPLDSSPHQ 360  
FSLTSPSLNLSLQAVTVVTKSLTASPKLSTQDAEDQALQSGQO 450  
LEQARQCTLLIAPLQKQPLVIGERVATSPRTVQKLPKRPLSKTQSPPLQSPQALQOQVHQOQOQOQOQOQOQOQOQOQOQOQO 540  
LPRQPTTPESTEELTEQOVLGECALDHPREGTESESTQEDLEEDDEEDCEEEDCIQVKDEEGSCAEQGPOLKEPGAGYQGLF 630  
SDAQPLQVQVQAPLSLATVPHQALQKQSSPAAPQOQKSPQOQVQHLFTTGVVYDTPLHQKQKQNTBVRHGRKIQSIHSLQ 720  
TGLLSKCERIRGRATLDEIQTVHSEYHLLFTGTPMLRQKLESKOLLGPIQOQVAVLPQCGTGVSDTVHMDHSSAVHAGCLLE 810  
LAFVAVGELQNGFATIRPKBAESTAGKCFPMVATIKELQOQLNVCGLVIVMDHIREGNGTQAVTNDPSVLYTSLRYDQKMF 900  
FPGSCAPLEVCCTGCVGCVHNAVATGCVPIIGDVEYLAFTVMPPIAHEFSKQVVLVSAGFADAVEGSLPLGGTSTVATCFGLTRQ 990  
MLAGCRVLALEGGDLTALCDASEACVSALLSVELQPLDEAVLQKQKMINAVATLEKVTIQSIHNSCVQKFAGLGRSLRENGCT 1080  
EEAETVSVAALLSVCAEQAAQAAAARHISPRFAEPHEQEPAL. 1123

C. HDAC6

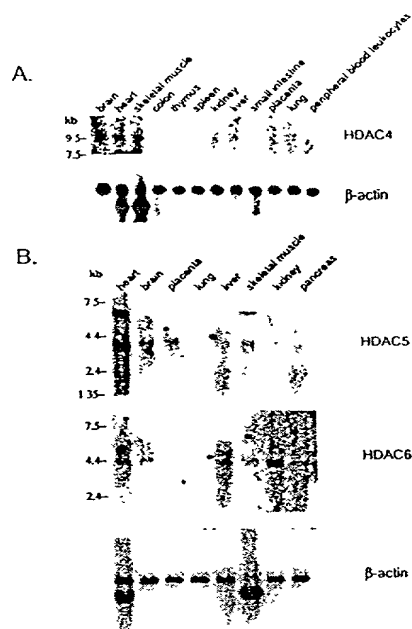
MTSTQDSTTTRQRSRQNSQSPPOQSVTSKNIIXKAVPRSIPLAEVQKQKXKQLQAEEDLVLQOQDLNLEAEALAGTGLVL 90  
DEQLMEFRCMDOSFTQEPERLPAIXEQLIQELLDRCVSFAEKEELMLVHSLEYIDMETTQVNEGELRVLATYDSVLYPHNS 180  
YSACLASGSLRLVDAVLQAEIRHQAIIIRPPCBHAQSLSHOCYCFHVAVAARYAQOQIRIRRVLIIVMDVIBGNGTQFTTQDDPSV 270  
LYFSIRRYEQGRFPHLKASNNSTTCGQOQGYTINVMHQVGRDADYIAAFLHVLVPALEFQOQVLVANGFDALQGDPKGHAATP 360  
AGFAGLTHLWCLAGCKLILSLDGYMLRALAGVSASLHTLGDPCHELSPOACRASAQVSICALALEPFVEVLVASTETVERBM 450  
IEEWVEESEEGPMEFPLPILTHVPLQKQCTGVDQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 540  
SANYVGRBATEQKREILRESSMDSIYICPSTFACQALATGAACRLVEANLSCEVLKQAAVVRPGBRAEQOQACGCFPHNSVAA 630  
RHQVTSIGUALRILIVMDVIBGNGTQOQFEDDPSVLYSLRYDNGTTFPHGDEGASSQIGRAAGTGFTVNVAMGPRMGDADYLAAMH 720  
RLVLPIAYEFNPELVLSAGFADARCDPLGQCVSPEGYNHLTHLKLASGRIILILEGGYNLTSISESHAACTRSLLGDPPLTLPR 810  
PPLSCALASITETIQVHRYNRSLRVMDVIBGNGTQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 900  
AVVATLQOQPSAEATGATLQATISDAATGCVLQGTTESEAVGATPQOQSTSEETVQKILDGTISEDAVGCATLQGTSEAVGATL 990  
AQITISEANDECATLQGTTESEAVGATLQGTTESEAVGATLQGTTESEAVGATLQGTTESEAVGATLQGTTESEAVGATLQGTTESEAV 1080  
ACQOQADGSLHMQSGRLTQAIIFYAVTLPKCHLVAVCP1PAGLDVTOPCGDGTIQEMWCLSCYQVYCRYINGHMLQHQNSGH 1170  
PLVLSYLDLSAWCTYQAVYHQAALLDQVHIAHQNGFEDHPRH. 1216

D.

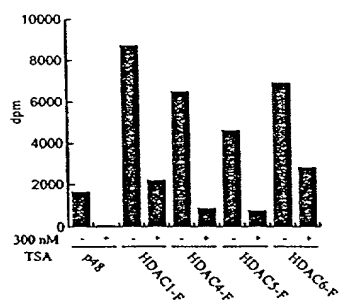
HDAC1 140 HAAKXSEASGFCYVNDIVLAILLELYR- - - QRVLYTIDIDIRRGCGVEEAFPTTDRVHTVAFBKY- - GYFFPGT 208  
HDAC4 802 HAAKESTPHGFCYFMSVAVAAKLLQORLSVS- - X-ILVMDVIBGNGTQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 874  
HDAC5 832 HAAKESTAHGFCYFMSVAVAAKLLQORLSVS- - X-ILVMDVIBGNGTQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 896  
HDAC6 215 HAAKESLHDDTCYFMSVAVAAKLLQORLSVS- - X-ILVMDVIBGNGTQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 287  
HDAC6 610 HAAKESLHDDTCYFMSVAVAAKLLQORLSVS- - X-ILVMDVIBGNGTQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 682  
HDAC6 205 HAAEPQAAAGCTCLFMSVAVAAKLLQORLSVS- - X-ILVMDVIBGNGTQOQPHRCLMDQSHRVEVPORILRIMCRLLEELGACRCLTLYPRPATELLETCR 279

FOOOOT" 28FOO860

Figure 2



A.



B.

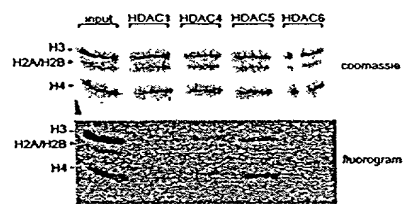
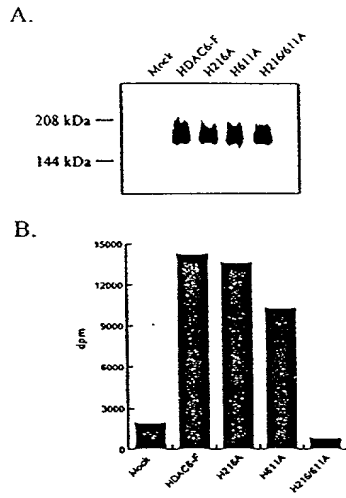


Figure 3

Figure 4



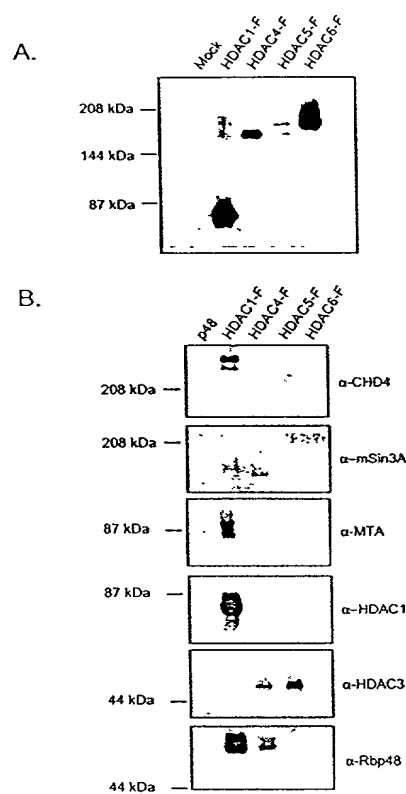


Figure 5

[illegible]

B.

Phylogenetic tree showing the relationships between various HDACs and related proteins. The tree is rooted with a question mark. The x-axis represents a scale from 20 to 1. The proteins listed are HDAC1, HDAC2, Rpd3p, HDAC3, Hos2p, Hos1p, pcvC, HDAC4, HDAC5, HDAC6 (AA 1-416), HDAC6 (AA 416-1216), Hda1p, ASD, and Hos3p.

Figure 7

Figure 7A

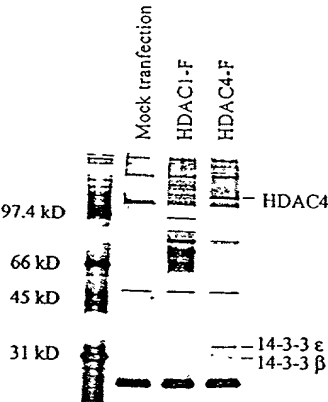


Figure 7B

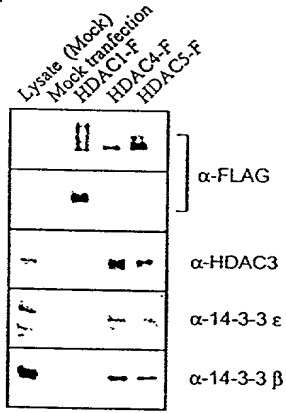


Figure 8

Figure 8A

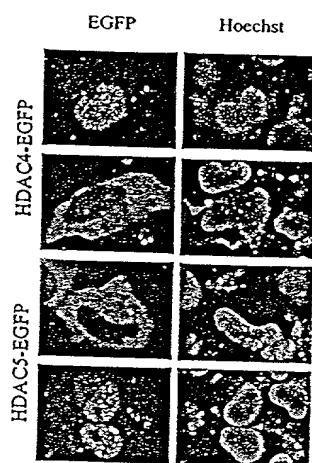
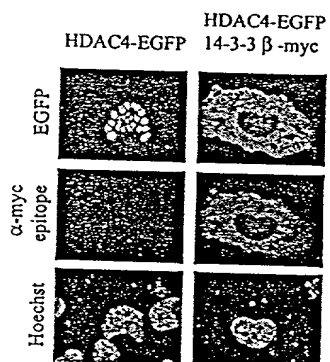


Figure 8B





106001-28100860

Figure 9

Figure 9A

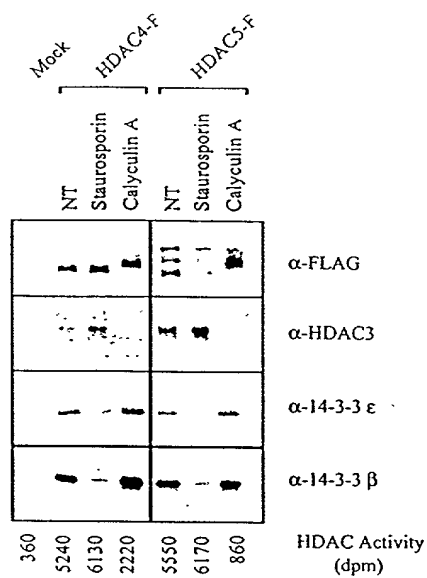


Figure 9B

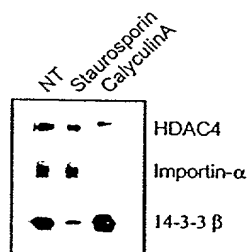




Figure 11

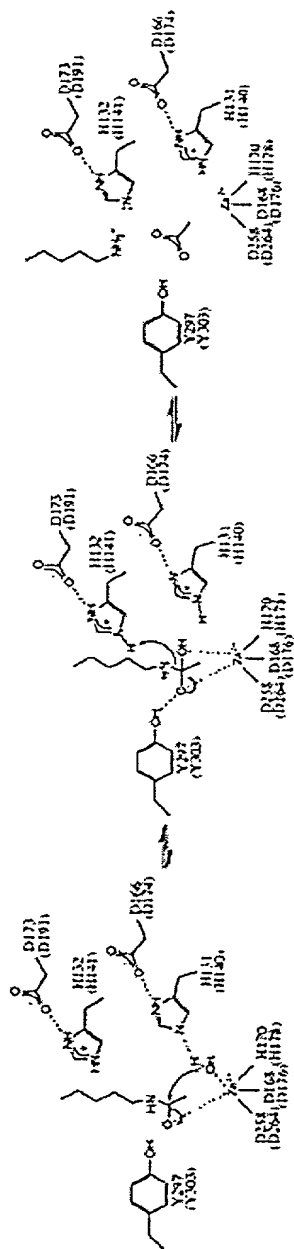


Figure 12

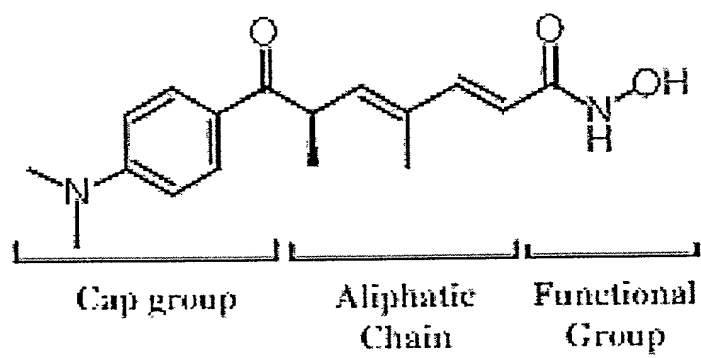
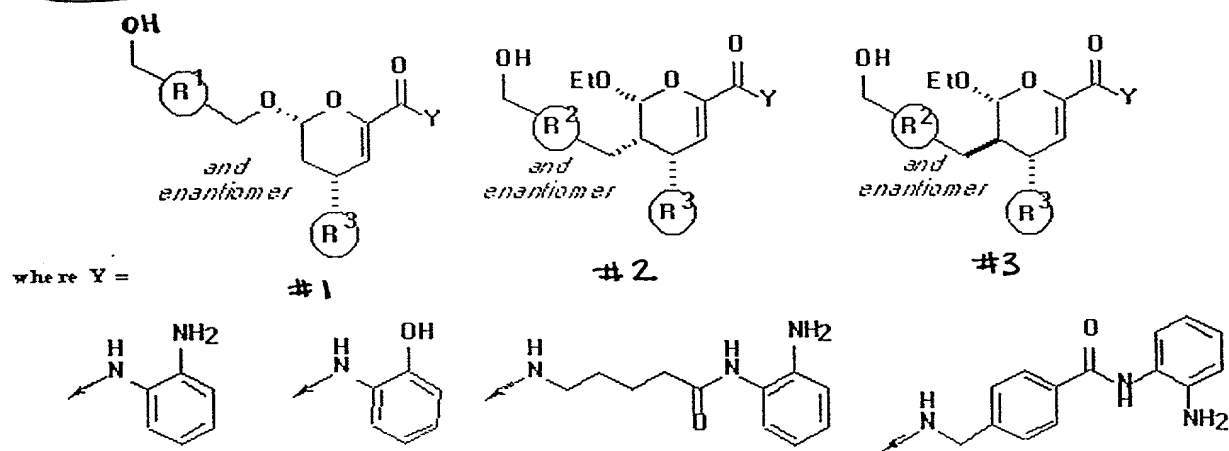


Figure 13

		Residues on rim of channel				Residues in channel			
		12*	11	10	9	3	2	1	126
Class I	HDLP	P	I	G	G	Y	E	N	P
	HDAC1	P	N	G	-	E	D	C	P
	HDAC2	P	N	G	-	E	D	C	P
	HDAC3	P	N	G	-	O	D	C	P
	HDAC4	A	K	G	-	Y	D	C	P
	HDAC5	P	I	G	V	D	S	D	T
	HDAC6(a)	P	I	-	-	-	-	D	S
Class II	HDAC6(b)	P	I	-	-	-	-	D	S
	HDAC7	P	I	G	V	D	T	D	T
		12*	11	10	9	3	2	1	126
Class I	HDLP	N	G	I	-	E	-	Y	A
	HDAC1	S	G	I	-	E	-	Y	F
	HDAC2	S	G	I	-	E	-	Y	F
	HDAC3	S	G	I	-	N	-	Y	F
	HDAC4	S	G	I	-	D	-	G	F
	HDAC5	N	G	I	-	D	G	N	F
	HDAC6(a)	D	G	I	-	N	G	N	F
Class II	HDAC6(b)	D	G	I	-	Q	G	R	F
	HDAC7	C	G	I	-	N	G	T	F
		126	125	124	123	122	121	120	119
Class I	HDLP	Y	I	D	I	N	A	H	C
	HDAC1	Y	I	D	I	N	A	H	C
	HDAC2	Y	I	D	I	N	A	H	C
	HDAC3	Y	I	D	I	N	A	H	C
	HDAC4	Y	I	D	I	N	A	H	C
	HDAC5	Y	I	D	I	N	A	H	C
	HDAC6(a)	Y	I	D	I	N	A	H	C
Class II	HDAC6(b)	Y	I	D	I	N	A	H	C
	HDAC7	Y	I	D	I	N	A	H	C
		118	117	116	115	114	113	112	111
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		110	109	108	107	106	105	104	103
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		102	101	100	99	98	97	96	95
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		93	92	91	90	89	88	87	86
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		83	82	81	80	79	78	77	76
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		73	72	71	70	69	68	67	66
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		63	62	61	60	59	58	57	56
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		53	52	51	50	49	48	47	46
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		43	42	41	40	39	38	37	36
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		33	32	31	30	29	28	27	26
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		23	22	21	20	19	18	17	16
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		13	12	11	10	9	8	7	6
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		3	2	1	0	-1	-2	-3	-4
Class I	HDLP	P	A	G	G	N	H	H	A
	HDAC1	P	A	G	G	N	H	H	A
	HDAC2	P	A	G	G	N	H	H	A
	HDAC3	P	A	G	G	N	H	H	A
	HDAC4	P	A	G	G	N	H	H	A
	HDAC5	P	A	G	G	N	H	H	A
	HDAC6(a)	P	A	G	G	N	H	H	A
Class II	HDAC6(b)	P	A	G	G	N	H	H	A
	HDAC7	P	A	G	G	N	H	H	A
		-5	-6	-7	-8	-9	-10	-11	-12

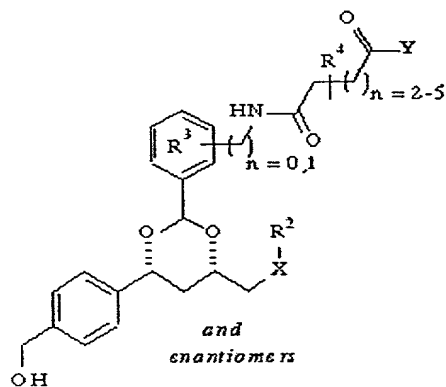
Figure 14

14A



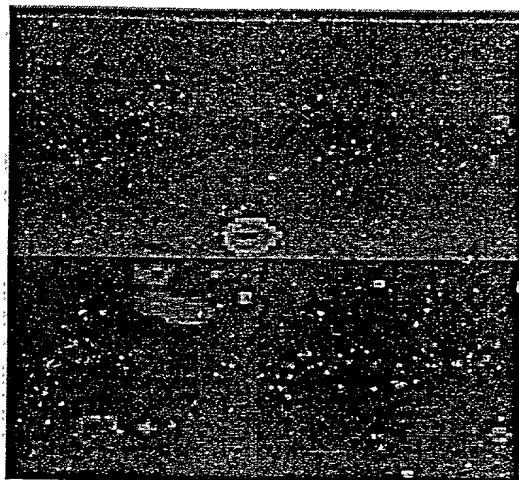
[4 R<sup>1</sup> groups + 2R<sup>2</sup> groups] ↔ 10 R<sup>3</sup> groups ↔ 2 (enantiomers) ↔ 4 amines = 640 compounds

14B



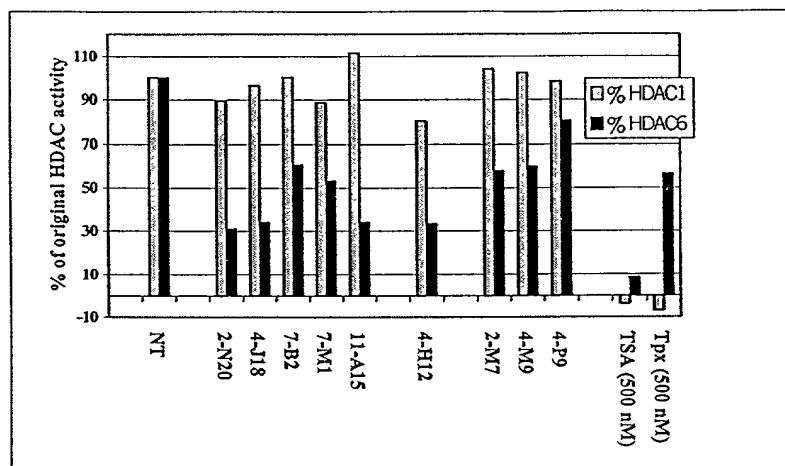
where Y = OH, NHOH, o-aminoaniline

Figure 15



09800187 100901

Figure 16



09200387 . 100903



Figure 17

